Virtual 3D heart models to aid pacemaker implantation in children

Natalia A Trayanova[*]

[*]Department of Biomedical Engineering & Institute for Computational Medicine, Johns Hopkins University, Baltimore, MD, USA; ntrayanova@jhu.edu

Keywords

congenital heart disease; defibrillation threshold; device implantation; electric shock; finite element modeling; image-processing pipeline; implantable cardioverter–defibrillator; pediatric patient; virtual heart model

Defibrillation by a strong electric shock remains the only known effective way of terminating ventricular fibrillation and thus preventing sudden cardiac death. External defibrillators have long been used as standard therapy, and implantable cardioverter–defibrillators (ICDs), based on mature foundational technology that evolved from antibradycardia pacing, have also been demonstrated to be an effective, life-saving technology. Large, well-controlled prospective ICD therapy trials such as AVID, MADIT-I and -II, and MUST have revolutionized the concept of sudden cardiac death prophylaxis and have proven the efficacy of ICDs for both secondary and primary prevention of sudden cardiac death [1]. These studies have led to the rapid growth of patient populations for whom ICDs are indicated, with over 110,000 devices implanted annually in the USA alone.

As a result, increasingly diverse populations of patients have been undergoing ICD implantation. In 1989, the first use of ICDs in young patients was reported [2]. Since then, ICD therapy has become increasingly important as a treatment approach in the pediatric population [3], with the mean age at implant decreasing significantly (from 13.6 to 12.2 years), and the percentage of patients younger than 5 years of age receiving an ICD increasing to above 10% [4]. The clinical outcome of ICD therapy in pediatric patients and adults with congenital heart disease has been evaluated by large multi-center studies, which included more than 200 children [5,6].

Despite the increased ICD implantation rate and the successes in ICD therapy, children and patients of small body size, as well as patients with congenital heart disease, are poorly served by current ICD technology. In these populations, the procedural approach and site of implantation, therapeutic algorithms, and early and long-term complications are different from those in adults, and the optimal ICD implantation technique has not yet been established. Furthermore, transvenous approaches to lead implantation presents a problem because of the small venous system [7] – there are no specific electrodes for small vessel

diameters – and because of the frequent congenitally altered heart anatomy. As a result, transvenous approaches are associated with an increased risk of venous thrombosis. Nontransvenous ICD systems used currently in clinical practice in younger patients and in those with smaller body surface area, intracardiac shunts, and concurrent thoracotomy surgery or affection of tricuspid valve include pericardial and subcutaneous coils. In addition, existing ICD devices are not adapted to the pediatric patient's small body surface and weight, frequently requiring abdominal implantation of the power generator. Early physical activity and impaired sterile conditions lead to more frequent procedural complications in these patient populations. Inappropriate discharges, lead-related complications and generator anomalies are the most common adverse events occurring during follow-up; Lewandowski *et al.* reported a 21% rate of complications requiring surgical intervention [

The variability and structural complexity of pediatric hearts, particularly those with congenital heart defects, make ICD device implantation and management a highly individualized art. There is currently no reliable, personalized way of predicting which ICD configuration would have the lowest defibrillation and/or cardioversion thresholds in such a patient. A wide variety of innovative approaches to ICD implantation have been demonstrated to be clinically feasible in children and congenital heart patients. These approaches have generally utilized 'off-the-shelf' technology in untested ways. Little data are available to guide the specific application of defibrillation strategies in these patient groups. Clinical studies in these patient groups to determine appropriate defibrillation parameters are difficult to design and complete due to ethical and practical considerations. The clinical data indicate that because ICD technology is deployed into clinical situations for which it has been neither designed nor extensively validated by clinical experience, there is now a pressing need for alternative approaches to technology development and therapy planning in the field of cardiac defibrillation, approaches that are both flexible and incorporate our increased knowledge of the mechanisms by which an electric shock defibrillates the heart.

By marrying clinical MRI with sophisticated computer analysis, the paper by Rantner *et al.* has now provided proof of concept that it is possible to take the guesswork out of the ICD implantation process in pediatric and congenital heart disease patients [9]. The researchers used an MRI-based patient-specific 3D heart–torso model that takes into account the child's unique heart anatomy, and determined the optimal locations (in terms of minimum shock energy) for both leads and the power generator before the device is implanted.

In the past, finite element modeling has been used by numerous investigators to model human defibrillation. Specifically, models of the human thorax have been employed to predict the intensity of an electrical field delivered by a defibrillator device, as well as the amount of current that reaches the heart during this process. Attempts to construct heart–torso models from MRI data sets have also been made previously, but only for patients with structurally normal hearts. Such models have been employed in the study of defibrillation [10–13], as well as for other uses [14]. However, all of these prior models were limited to predicting only the static thoracic electrical field induced by the electric shock, and relied on inference to predict the actual electrophysiological effect of this field on the fibrillating

heart. To adequately describe this response, it is necessary to include in these models a biophysically accurate, mechanistic representation of the interaction of the defibrillation electric field with the myocardium.

Studies have demonstrated that the cells in the heart respond to the electric current delivered by the defibrillator device in a strongly nonlinear fashion, by generating concurrent regions of positive and negative membrane polarization throughout cardiac tissue [15,16]. This effect is termed 'virtual electrode polarization' (VEP) and represents the essence of the interaction between cardiac tissue and the applied electric field. VEP has been documented in numerous experimental studies and is supported by computer simulations [17–19]. Furthermore, research has shown that in addition to the nonlinear membrane response, cardiac tissue structure, particularly fiber architecture, plays an important role in the generation of VEP and its shape, location, polarity and intensity [20]. The distribution of VEP throughout the heart in response to the shock determines whether existing wave fronts in the heart are terminated by the shock, and whether new wave fronts are generated that could reinitiate arrhythmia. Clearly, accurate prediction of the generation of VEP and subsequent propagation of postshock activation is necessary for the accurate prediction of shock outcome, and requires explicit representation of both the electrophysio logical properties of the myocardium, as well as the myocardial geometry and fiber architecture.

The study by Rantner *et al.* presented the first electrophysiological, active multiscale heart–torso model that accounted for the aforementioned interactions between an applied electric field and the cells in the heart [9]. Importantly, the study developed a new image-processing pipeline for building patient-specific heart–torso models from low-resolution clinical MRIs, which was applied, in a proof of principle, to a pediatric patient with congenital heart disease. Using the pediatric patient heart–torso model constructed with this image-processing pipeline, the study used simulations of the defibrillation process to determine the shock outcome for different ICD configurations. Ventricular fibrillation was induced in the model heart, and defibrillation shocks were applied from 11 ICD configurations to determine the outcomes of shocks and the defibrillation thresholds, the minimum amount of energy that successfully defibrillated the heart with shocks from a given ICD configuration. Two configurations with epicardial leads resulted in the lowest defibrillation thresholds overall and were, thus, considered optimal. The study also demonstrated that in order to reliably predict defibrillation outcome, the patient-specific heart model needs to accurately incorporate the biophysically detailed interaction between the applied shock and the cells of the heart. The pipeline and methodology developed in this study presented a novel approach to predicting the optimal ICD configurations before device implantation, a tool of particular importance, as reviewed above, for pediatric and congenital heart disease patients who have contraindications for transvenous lead ICD implantation. The clinical translation of this approach could provide a reliable, personalized way of predicting the location of ICD device placement in such patient populations.

Acknowledgments

manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Biography

References

1. Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter automatic defibrillator implantation trial investigators. N. Engl. J. Med. 1996; 335:1933–1940. [PubMed: 8960472]

2. Kral MA, Spotnitz HM, Hordof A, Bigger JT, Steinberg JS, Livelli FD. Automatic implantable cardioverter–defibrillator implantation for malignant ventricular arrhythmias associated with congenital heart disease. Am. J. Cardiol. 1989; 63:118–119. [PubMed: 2909142]

3. Silka MJ, Kron J, Dunnigan A, Dick M 2nd. Sudden cardiac death and the use of implantable cardioverter–defibrillators in pediatric patients. The Pediatric Electrophysiology Society. Circulation. 1993; 87:800–807. [PubMed: 8443901]

4. Burns KM, Evans F, Kaltman JR. Pediatric ICD utilization in the United States from 1997 to 2006. Heart Rhythm. 2011; 8:23–28. [PubMed: 20887811]

5. Berul CI, Van Hare GF, Kertesz NJ, et al. Results of a multicenter retrospective implantable cardioverter–defibrillator registry of pediatric and congenital heart disease patients. J. Am. Coll. Cardiol. 2008; 51:1685–1691. [PubMed: 18436121]

6. Von Bergen NH, Atkins DL, Dick M 2nd, et al. Multicenter study of the effectiveness of implantable cardioverter–defibrillators in children and young adults with heart disease. Pediatr. Cardiol. 2011; 32:399–405. [PubMed: 21210096]

7. Radbill AE, Triedman JK, Berul CI, et al. System survival of nontransvenous implantable cardioverter-defibrillators compared with transvenous implantable cardioverter–defibrillators in pediatric and congenital heart disease patients. Heart Rhythm. 2010; 7:193–198. [PubMed: 20022820]

8. Lewandowski M, Sterlinski M, Maciag A, et al. Long-term follow-up of children and young adults treated with implantable cardioverter–defibrillator: the authors' own experience with optimal implantable cardioverter–defibrillator programming. Europace. 2010; 12:1245–1250. [PubMed: 20650939]

9. Rantner LJ, Vadakkumpadan F, Spevak PJ, Crosson JE, Trayanova NA. Placement of implantable cardioverter–defibrillators in paediatric and congenital heart defect patients: a pipeline for model generation and simulation prediction of optimal configurations. J. Physiol. 2013 doi:10.1113/jphysiol.2013.255109. (Epub ahead of print).

10. Eason J, Schmidt J, Dabasinskas A, Siekas G, Aguel F, Trayanova N. Influence of anisotropy on local and global measures of potential gradient in computer models of defibrillation. Ann. Biomed. Eng. 1998; 26:840–849. [PubMed: 9779957]

11. de Jongh AL, Entcheva EG, Replogle JA, Booker RS 3rd, Kenknight BH, Claydon FJ. Defibrillation efficacy of different electrode placements in a human thorax model. Pacing Clin. Electrophysiol. 1999; 22:152–157. [PubMed: 9990621]

12. Jolley M, Stinstra J, Pieper S, et al. A computer modeling tool for comparing novel ICD electrode orientations in children and adults. Heart Rhythm. 2008; 5:565–572. [PubMed: 18362024]

13. Jolley M, Stinstra J, Tate J, et al. Finite element modeling of subcutaneous implantable defibrillator electrodes in an adult torso. Heart Rhythm. 2010; 7:692–698. [PubMed: 20230927]

14. Vanheusden F, Loures Salinet J, Nicolson WB, McCann GP, Ng GA, Schlindwein FS. Patient-specific three-dimensional torso models for analysing cardiac activity. Comput. Cardiol. 2012; 2012:973–976.

15. Efimov IR, Cheng Y, Yamanouchi Y, Tchou PJ. Direct evidence of the role of virtual electrode-induced phase singularity in success and failure of defibrillation. J. Cardiovasc. Electrophysiol. 2000; 11:861–868. [PubMed: 10969748]

16. Trayanova N. Concepts of ventricular defibrillation. Phil. Trans. R. Soc. Lond. A. 2001; 359:1327–1337.

17. Rodríguez B, Li L, Eason J, Efimov I, Trayanova N. Differences between left and right ventricular chamber geometry affect cardiac vulnerability to electric shocks. Circ. Res. 2005; 97:168–175. [PubMed: 15976315]

18. Efimov IR, Cheng Y, Van Wagoner, David R, Mazgalev TN, Tchou PJ. Virtual electrode-induced phase singularity: a basic mechanism of defibrillation failure. Circ. Res. 1998; 82:918–925. [PubMed: 9576111]

19. Efimov IR, Cheng YN, Biermann M, Van Wagoner DR, Mazgalev TN, Tchou PJ. Transmembrane voltage changes produced by real and virtual electrodes during monophasic defibrillation shock delivered by an implantable electrode. J. Cardiovasc. Electrophysiol. 1997; 8:1031–1045. [PubMed: 9300301]

20. Trayanova N, Skouibine K, Aguel F. The role of cardiac tissue structure in defibrillation. Chaos. 1998; 8:221–233. [PubMed: 12779723]

"By marrying clinical MRI with sophisticated computer analysis, the paper by Rantner *et al.* has now provided proof of concept that it is possible to take the guesswork out of the implantable cardioverter–defibrillator implantation process in pediatric and congenital heart disease patients.**"**

> **"**Despite the increased implantable cardioverter–defibrillators (ICDs) implantation rate and the successes in ICD therapy, children and patients of small body size, as well as patients with congenital heart disease, are poorly served by current ICD technology.**"**

"There is currently no reliable, personalized way of predicting which implantable cardioverter–defibrillator configuration would have the lowest defibrillation and/or cardioversion thresholds in such a patient."